

Amendments to the Specification

At page 2, line 6, please insert the following replacement paragraph:

Bactericidal permeability-increasing protein (BPI), is a protein isolated from the granules of mammalian polymorphonuclear neutrophils (PMNs). Human BPI has been isolated from PMNs by acid extraction combined with chromatography (Elsbach, 1979, *J. Biol. Chem.* 254:11000; Weiss et al. 1987, *Blood* 69:652), and has been shown to have potent bactericidal activity against a broad spectrum of Gram-negative bacteria. In addition to its bactericidal effect on Gram negative bacteria, BPI is also capable of binding to and neutralizing lipopolysaccharide (LPS) which is also known as ~~endotoxin~~endotoxin because of the inflammatory response that it stimulates.

At page 3, line 5, please insert the following replacement paragraph:

Most of the damage comes not from the invading bacteria but from endotoxin. This effect by ~~enotoxin~~endotoxin is manifested by its binding to cells such as monocytes/macrophages or endothelial cells, and triggering them to produce various mediators such as tumor necrosis factor-alpha (TNF-a), and various interleukins (IL-1, IL-6, and IL-8). Production of excessive TNF-a, IL-1, IL-6, and IL-8 can elicit septic shock.

At page 4, line 6, please insert the following replacement paragraph:

Recombinant BPI protein has been shown to neutralize lethal and sublethal effects of endotoxin administered to mice, rats, and rabbits (Fisher, et al., *Crit. Care Med.*, 22(4): 553-558, 1994). Because of this ability to neutralize endotoxin and its Gram-negative ~~bacteriacidal~~bactericidal

activity, BPI can be utilized for the treatment of human patients suffering from diseases caused by gram-negative bacteria , including bacteremia, endotoxemia, and sepsis.

At page 10, line 22, please insert the following replacement paragraph:

The phrase "in combination with" refers to the administration of BPI protein with protein C either simultaneously, sequentially or a combination thereof. The BPI protein utilized and the appropriate dose level is known in the art and described in U.S. Patent No. 5,756,464, herein incorporated by reference. A skilled artisan recognizes the appropriate dose level to use to achieve a pharmaceutically effective amount for treating sepsis. Pharmaceutically effective compositions comprising BPI protein may be administered systemically or topically. Systemic routes of administration include, intravenous, intramuscular or subcutaneous injection (including into a depot for long-term release), intraocular and retrobulbar, intrathecal, intraperitoneal (e.g. by intraperitoneal lavage), intrapulmonary using ~~aerosolezed~~aerosolized or nebulized drug, or transdermal. The preferred route is intravenous administration. When given parenterally, BPI protein compositions are generally injected in doses ranging from about 0.04 ug/kg/hr to about 4 mg/kg/hr. Preferably, the BPI protein is administered at about 4 ug/kg/hr to about 420 ug/kg/hr. More preferably the BPI protein is administered at about 50 ug/kg/hr to about 300 ug/kg/hr. Even more preferably the BPI protein is administered at about 100 ug/kg/hr to about 200 ug/kg/hr. The treatment may continue by continuous infusion or intermittent injection or infusion, at the same, reduced or increased dose per day for, e.g. 24 hours to 240 hours, and additionally as determined by the treating physician. BPI protein is preferably administered intravenously by an initial bolus injection

followed by a continuous infusion. A preferred dosing regimen is about 0.1 mg/kg to about 10 mg/kg intravenous bolus of BPI protein followed by intravenous infusion at about 4 ug/kg/hr to about 420 ug/kg/hr, continuing for up to 10 days. Those skilled in the art can readily optimize pharmaceutically effective dosages and administration regimens for therapeutic compositions comprising BPI protein, as determined by good medical practice and the clinical condition of the individual patient.